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Basiliximab in pediatric liver transplantation: a pharmacokinetic-derived dosing algorithm.

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The pharmacokinetics and immunodynamics of basiliximab were assessed in 37 pediatric de novo liver allograft recipients to rationally design a dose regimen for this age-group. In part one of the study, patients were given 12 mg/m2 basiliximab by bolus intravenous injection after organ perfusion and on day 4 after transplant. An interim pharmacokinetic evaluation supported a fixed-dose approach for part two of the study in which infants and children received two 10-mg doses of basiliximab and adolescents received two 20-mg doses. Blood samples were collected over a 12-week period for screening for anti-idiotype antibodies and analysis of basiliximab and soluble interleukin-2 receptor (IL-2R) concentrations. Basiliximab clearance in infants and children < 9 yr of age (n = 30) was reduced by approximately 50% compared with adults from a previous study and was independent of ag to 9 yr, weight to 30 kg, and body surface area to 1.0 m2. Clearance in children and adolescents 9-14 yr of age (n = 7) approached or reached adult values. An average of 15% of the dose was eliminated via drained ascites fluid, and drug clearance via this route averaged 29% of total body clearance Patients with > 5 L of ascites fluid drainage tended to have lower systemic exposure to basiliximab. CD25-saturating basiliximab concentrations were maintained for 27 +/- 9 days in part one of the study (mg/m2 dosing) with infants exhibiting the lowest durations. CD25 saturation lasted 37 +/- 11 day in part two of the study, based on the fixed-dose regimen (p = 0.004 vs. mg/mg2 dosing), but did not show the age-related bias observed in part one of the study. Anti-idiotype antibodies were detected in four patients, but this did not influence the clearance of basiliximab or duration of CD25 saturation All 40 enrolled patients were included in the intent-to-treat clinical analysis. Episodes of acute rejection occurred in 22 patients (55%) during the first 12 months post-transplant. Three patients experienced loss of their graft as a

result of technical complications, and six patients died during the 12-month study. Basiliximab was well tolerated by intravenous bolus injection, with nc cytokine-release syndrome or other infusion-related adverse events. Hence, basiliximab was safe and well tolerated in pediatric patients undergoing orthotopic liver transplantation. To achieve similar basiliximab exposure as i efficacious in adults, pediatric patients < 35 kg in weight should receive two 10-mg doses and those > or = 35 kg should receive two 20-mg doses of basiliximab by intravenous infusion or bolus injection. The first dose should be given within 6 h after organ perfusion and the second on day 4 after transplantation. A supplemental dose may be considered for patients with a large volume of drained ascites fluid relative to body size.

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